Helicobacter Pylori Eradication Has No Effect on Metabolic and Inflammatory Parameters

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Background: An increased risk in coronary heart disease associated with *Helicobacter pylori* (*H. pylori*) appears to be partially mediated by modifications of the atherogenic lipoprotein and inflammatory parameters. We conducted a controlled trial aimed at evaluating the changes of metabolic and inflammatory parameters after *H. pylori* eradication.

Methods: We included in the study 169 patients with *H. pylori* infection and conducted a retrospective longitudinal survey of 87 subjects (76 men, 11 women) who received treatment for *H. pylori* eradication and 82 control subjects (63 men, 19 women) who did not receive treatment. We compared pre- and posteradication (one year after) the metabolic and inflammatory parameters, such as blood sugar, lipid profiles, insulin resistance, white blood cell count and C-reactive protein.

Results: No significant changes from the baseline in metabolic and inflammatory parameters within each group were observed. Changes in the serum levels of metabolic and inflammatory parameters were similar between the two groups.

Conclusions: Metabolic and inflammatory parameters, including blood sugar, lipid profiles, insulin resistance, white blood cell count and C-reactive protein, were not changed after *H. pylori* eradication treatment. *H. pylori* eradication has no effect on metabolic and inflammatory parameters.

Key words: *Helicobacter pylori* ■ eradication ■ coronary heart disease

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INTRODUCTION

Several epidemiologic studies have shown that the presence of *Helicobacter pylori* (*H. pylori*) is associated with coronary heart disease and its risk factors.[1-3] Although a number of studies concerning this relationship with *H. pylori* have reported conflicting results,[4-6] the increased risk in coronary heart disease associated with *H. pylori* appears to be partially mediated by modifications of the atherogenic lipoprotein and inflammatory parameters.[7-10] A recent clinical study, lacking a control for confounding factors, reported that *H. pylori* eradication improves the lipoprotein pattern.[11] Based on these previous studies, we conducted a controlled trial aimed at evaluating the changes of metabolic and inflammatory parameters after *H. pylori* eradication.

MATERIALS AND METHODS

Subjects

This study is a nonrandomized longitudinal study that was assembled retrospectively. Subjects who visited the medical screen center of the Kangbuk Samsung Hospital for gastrointestinal screening were investigated between January 2002 and October 2003. Of these, 87 patients had a peptic ulcer disease with *H. pylori* infection and revisited the medical screen center for a regular medical check-up one year after a successful eradication treatment. During the initial endoscopy, four specimens were obtained from the antrum and corpus of each subject. The two specimens from the antrum were used to assess the *H. pylori* status by a rapid urease test (CLO test, Medical Instruments Corp., Solothurn, Switzerland). The two specimens from the corpus were fixed in 10% buffered formalin and embedded in paraffin for histology. *H. pylori* infection was diagnosed positive when a confirming result was obtained from any of the tests, then eradicated by triple therapy, which comprised of a seven-day course using a proton pump inhibitor and two antibiotics (standard OAC regimen; 20 mg omeperazol-1,000 mg amoxicillin-500 mg

clarithromycin). A follow-up endoscopy was performed six weeks after the last dose of medication. *H. pylori* eradication was defined as the absence of *H. pylori* in the rapid urease test and by histological assessment. We excluded subjects who showed evidence of taking current medications with lipid lowering agents or anti-inflammatory properties, an underlying chronic disease (cardiovascular disease, liver and renal failure, pulmonary disease), an acute infection, or who had a previous history of diabetes or fasting hyperglycemia.

Eighty-two controls were selected from consecutive subjects with a peptic ulcer disease and with *H. pylori* infection, and who were evaluated between the same time period as the eradication group. Although eradication of *H. pylori* was recommended, these subjects did not receive eradication of *H. pylori* but revisited the medical screen center one year after initial endoscopy. A close interview regarding their *H. pylori* eradication history elsewhere was performed by one physician. We selected the controls that have never received eradication treatment.

Informed consent was obtained from each subject, and the study protocol, in accordance with the Helsinki Declaration, was approved by the Kangbuk Samsung Hospital Institutional Committee on Human Research.

Table 1. Baseline Values of Demographic Characteristics

	Control	Eradication	P Value
Age (Years)			
N	82	87	
Mean (SD)	46.0 (8.0)	44.7 (7.9)	0.312
Gender N (%)			
Male	63 (76.8%)	76 (87.4%)	0.106
Female	19 (23.2%)	11 (12.6%)	
Current Smoking N (%)			
Smoker	26 (31.7%)	29 (33.3%)	0.87
Non smoker	56 (68.3%)	58 (66.7%)	
Weight (kg)			
N	82	87	
Mean (SD)	67.4 (10.1)	69.3 (11.2)	0.277
Body Mass Index (kg/m²)			
N	82	86	
Mean (SD)	24.1 (2.5)	24.2 (3.1)	0.962
Waist Circumference (cm)			
N	72	84	
Mean (SD)	81.8 (8.2)	83.3 (9.3)	0.376

Anthropometrical and Laboratory Data

Body mass index (BMI) was calculated from the measured values of height and weight (kg/m²). Waist circumference was measured to the nearest 0.1 cm as the minimum circumference between the umbilicus and the xiphoid process.

Blood was taken from both the control and eradication groups after initial consultation. Fasting blood sugar was measured with the hexokinase method after a 12-hour fast, followed by the measurement of total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Triglycerides and total cholesterol were measured with the enzymatic calorimetric test, HDL-C was measured with the selective inhibition method and LDL-C was measured with the homogeneous enzymatic calorimetric test using the automatic analyzer (Advia 1650, Bayer, Fernwald, Germany). Apolipoprotein A-I and apolipoprotein B were measured by rate nephelometry (IMMAGE System, Beckman Coulter, CA). Lipoprotein(a) was determined in duplicate by ELISA using the Immunozym Lp(a) Kit (Progen Biotechnik GMBH, Heidelberg, Germany). CRP was assayed by particle-enhanced immunonephelometry using a BNTM System (N High-Sensitivity CRP, Dade Behring, Marburg, Germany). Results are expressed in milligrams per liter, and the limit of detection was 0.175 mg/L for measurements performed with a sample dilution of 1:20. The coefficients of variation for intraassay precision were 3.1% at 0.5 mg/L and 3.4% at a concentration of 2.1 mg/L, and were 2.5% at 0.5 mg/L and 2.1% at 2.1 mg/L for interassay reproducibility. Insulin was assayed by means of an immunoradiometric assay (Biosource, Belgium). There was no cross-reactivity with proinsulin. The intraassay coefficients of variation were 2.1–4.5%, and the interassay coefficients of variation for the quality controls were 4.7–12.2%. A homeostasis model assessment of insulin resistance (HOMA-IR) was computed using the following formula: (fasting insulin in μU/ml x fasting glucose in mmol/L)/ 22.5.[12]

Statistical Analysis

In order to detect a 5 mg/dL

difference (0 vs. 5 mg/dL increment) in HDL-C changes (final value minus baseline value) and with a power of 90%, 168 patients should be entered into the study. We included 169 patients (82 patients in the control group and 87 in the eradication group). All the data was statistically analyzed using the SPSS program (Version 10.0, Inc., Chicago, IL) for Windows®. Comparison of serum metabolic and inflammatory parameters before and after *H. pylori* eradication was performed. The Wilcoxon signed-rank tests were used for comparisons of baseline to follow-up results for an overall and within treatment group comparison. Differences of baseline values and changes between treatment groups were tested with the Mann-Whitney U test. A repeated-measures ANOVA was used for the controlling of body weight changes between treatment groups.

Table 2. Baseline Values of Metabolic Parameters

	Control	Eradication	P Value
WBC (per μL)			
N	82	87	
Mean (SD)	5691 (1136)	6262 (1835)	0.061
Insulin (μU/mL)			
N	66	68	
Mean (SD)	7.8 (2.6)	8.1 (3.8)	0.98
HOMA-IR			
N	66	68	
Mean (SD)	1.8 (0.8)	1.8 (0.9)	0.781
CRP (mg/L)			
N	39	30	
Mean (SD)	0.9 (1.1)	0.8 (0.9)	0.908
Glucose (mg/dL)			
N	82	87	
Mean (SD)	93.2 (16.1)	90.3 (13.4)	0.14
Total Cholesterol (mg/dL)			
N	82	87	
Mean (SD)	212.1 (38.7)	210.1 (35.7)	0.744
Triglycerides (mg/dL)			
N	82	87	
Mean (SD)	175.9 (110.9)	177.0 (192.9)	0.540
HDL-C (mg/dL)			
N	82	87	
Mean (SD)	54.2 (15.7)	52.7 (13.7)	0.926
LDL-C (mg/dL)			
N	76	79	
Mean (SD)	121.1 (34.2)	123.6 (27.1)	0.601
Lipoprotein-a (mg/dL)			
N	39	30	
Mean (SD)	15.4 (15.4)	13.2 (12.1)	0.718
Apo A-I (mg/dL)			
N	39	30	
Mean (SD)	122.4 (25.5)	114.7 (18.9)	0.157
Apo B (mg/dL)			
N	39	30	
Mean (SD)	111.7 (32.3)	106.1 (29.2)	0.517

WBC: white blood cell; HOMA-IR: homeostasis model assessment; CRP: C-reactive protein; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; Apo A-I and B, apolipoprotein A-I and B.

RESULTS

We included in the study 169 (139 men and 30 women) patients with a peptic ulcer disease and *H. pylori* infection. Tables 1 and 2 show the metabolic and inflammatory parameters, and baseline clinical findings. The mean age was 45.3 ± 8.0 years (range 22–68 years). There were no significant differences in all variables between the two groups. A significant weight gain occurred in both the control and eradication groups when compared to baseline values (Table 3), and this was consistent among the two groups (Figure 1). No changes were observed from the baseline in metabolic and inflammatory parameters within each group. Patients in the eradication group experienced a minor reduction in the white blood cell count, but this trend remained insignificant between the two groups after an adjustment of weight changes. Changes in serum levels of metabolic and inflammatory parameters were similar between the two groups (Table 4).

DISCUSSION

Overall, no clear improvement of metabolic and inflammatory parameters was identified upon longitudinal comparison within each group after *H. pylori* eradication. A more detailed analysis between the two groups led to the

conclusion that a clear level of improvement is not observed in all dimensions of the parameters. However, there is some possibility that the number of subjects who had C-reactive protein, lipoprotein and apolipoprotein are small and may therefore invalidate any significant findings. A recent uncontrolled study has shown a 25% increase of HDL-C at 52 weeks after an eradication treatment.[11] However, the lack of a control group in that study did not allow the authors to conclude whether the improved lipoprotein pattern occurred spontaneously or as a result of *H. pylori* eradication. *H. pylori* has been recognized to induce a persistent low-grade, acute-phase response to stimulate the synthesis of fibrinogen and other acute-phase proteins.[13] In addition, elevated levels of inflammatory cytokine were found in *H. pylori*-infected subjects.[14] Although *H. pylori* eradication can decrease the level of fibrinogen,[9,15] this phenomenon can be interpreted as an intrinsic anti-inflammatory activity of the macrolide in a short-term course of study.[16] It is worth noticing that serial samplings may reveal the accurate changes of inflammatory parameters during a relatively long-term period.

In the present study, we assessed anthropometrics and smoking status as covariates. Other factors, such as lifestyle and dietary habits, may contribute to changes of the metabolic and inflammatory parameters. In addition, the current study was a retrospective survey, which had a wide disparity in favor of the men. These are important aspects of the study warranting comment.

Interestingly, patients in the eradication group significantly gained weight from the baseline value, compared to those in the control group [1.8 kg (2.6%) vs. 1.1 kg (1.6%), p=0.043]. This observation is in line with a previous *H. pylori* eradication study,[17] and the relationship between weight gain and *H. pylori* eradication has been proposed to be due to the increase in the ghrelin level after *H. pylori* eradication.[18]

In contrast to evidence which suggests that a successful *H. pylori* eradication leads to favorable metabolic changes,[9,11,15] whether the eradication may serve additional benefit on the parameters is still a matter of discussion. In summary, metabolic and inflammatory parameters, including blood sugar, lipid profiles, insulin resistance, white blood cell count and C-reactive protein, were not changed after *H. pylori* eradication treatment. *H. pylori* eradication has no effect on metabolic and inflammatory parameters.

Table 3. Difference of Demographic Characteristics at One Year from Baseline

	Control	Eradication	P Value	P Value*
Weight (kg)				
N	82	87		
Mean (SD)	1.1 (2.0)	1.8 (2.7)	0.043	
Body Mass Index (kg/m²)				
N	82	86		
Mean (SD)	0.3 (0.7)	0.5 (0.9)	0.074	0.59
Waist Circumference (cm)				
N	20	27		
Mean (SD)	0.5 (3.4)	3.0 (3.9)	0.032	0.274

* P values were derived from repeated measures ANOVA controlling for changes of body weight.

Figure 1. Changes of weight in the control and eradication groups. One year of follow-up led to a significant weight gain in the control (p<0.001) and eradication (p<0.001) groups when compared to the baseline. In addition, this degree of weight gain was significantly different between the two groups (p=0.043). The circles reflect outliers; the whiskers reflect 95% confidence intervals; the box represents the 25th and 75th percentiles.

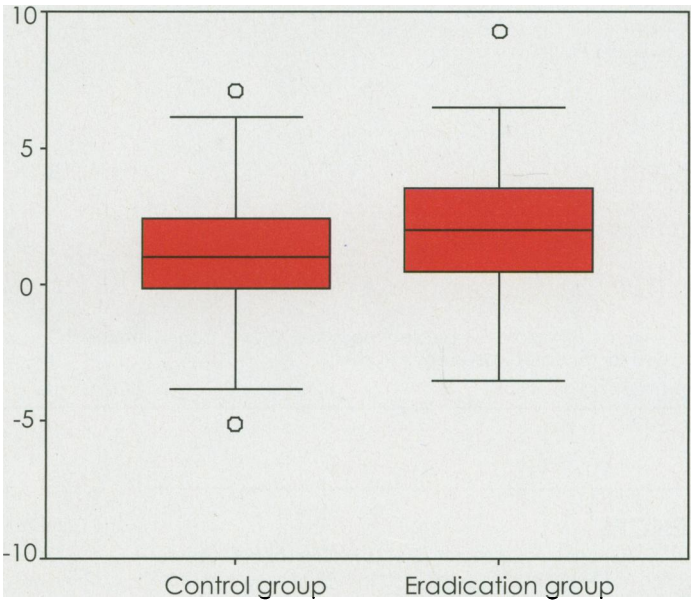

Table 4. Difference of Metabolic Parameters at One Year from Baseline

	Control	Eradication	P Value	P Value*
WBC# (per μL)				
N	82	87		
Mean (SD)	329.3 (1,415.0)	-299.7 (1,475.1)	0.037	0.301
Insulin (μU/mL)				
N	66	68		
Mean (SD)	-0.2 (2.7)	-0.4 (2.9)	0.852	0.591
HOMA-IR				
N	66	68		
Mean (SD)	0.02 (0.74)	0.02 (0.70)	0.705	0.952
CRP# (mg/L)				
N	35	29		
Mean (SD)	0.7 (2.5)	0.2 (1.3)	0.409	0.293
Glucose (mg/dL)				
N	82	87		
Mean (SD)	3.6 (8.6)	2.6 (9.0)	0.826	0.141
Total Cholesterol (mg/dL)				
N	82	87		
Mean (SD)	-1.1 (26.5)	4.6 (27.2)	0.121	0.695
Triglycerides (mg/dL)				
N	82	87		
Mean (SD)	-13.4 (82.4)	2.5 (73.8)	0.52	0.679
HDL-C (mg/dL)				
N	82	87		
Mean (SD)	-0.1 (10.7)	0.2 (10.0)	0.794	0.505
LDL-C (mg/dL)				
N	76	79		
Mean (SD)	-0.3 (23.0)	0.7 (22.6)	0.831	0.343
Lipoprotein-a# (mg/dL)				
N	35	29		
Mean (SD)	6.5 (12.8)	1.7 (5.6)	0.071	0.204
Apo A-I (mg/dL)				
N	35	29		
Mean (SD)	-6.7 (17.7)	-4.0 (18.9)	0.995	0.231
Apo B (mg/dL)				
N	35	29		
Mean (SD)	-6.5 (19.6)	3.8 (26.2)	0.235	0.987

* P values were derived from repeated measures ANOVA controlling for changes of body weight; # Values were logarithmically transformed for repeated measures ANOVA.

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